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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,708	03/11/2005	Hideki Matsui	Q101073	9989

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
12/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,708	MATSUI ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15 and 51-53* is/are pending in the application.

4a) Of the above claim(s) *51-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission and amendment filed on August 6, 2008, that includes a response to the office action dated June 11, 2008, has been entered. Claims 15 has been amended, claims 48-50 have been cancelled and claims 51-53 newly added. Accordingly, claims 15 and 51-53 are pending in the application.

Applicants should note that claim 15 was elected without traverse, and the subjected matter contained therein examined commensurate with the enabled scope previously indicated (i.e. a method comprising the step of hybridizing an antisense molecule or ribozyme to RNA of a gene encoding a protein comprising the amino acid sequence of SEQ ID NO: 1). However, newly presented claims 51-53 are directed to subject matter not previously examined, and would have been subject to restriction if earlier presented. While claims 51-53 share the same preamble as claim 15, each is directed to a separate method, having separate and distinct method steps, not required for the method of claim 15. For instance, claim 51 requires the step of adding a death inducer, claim 52 requires the step of assaying AKt1 protein binding, and claim 53 requires the step of measuring the expression of a reporter gene bearing NF-kB binding sequence. Further, the methods of new claims 51-53 do not require the step of assaying the degree of changes in nerve fivers, required for the method of claim 15. Thus, claims 51-53 have been withdrawn from consideration, as directed to non-elected inventions.

Claim 15 is under current examination.

Response & Withdrawn Claim Rejections - 35 USC § 112- New Matter

Claims 15 and 48-50 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, and introducing new matter, in the previous office action dated June 11, 2008. Applicants' cancellation of claims 48-50 renders their rejection moot. Applicants have amended claim 15 to remove the new matter, thus obviating the ground of rejection. Accordingly, the rejection is hereby withdrawn.

Response & Withdrawn Claim Rejections - 35 USC § 112, Written Description

Claim 15 was rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, in the previous office action dated June 11, 2008. Applicants have amended claim 15, deleting the limitation of "an amino acid sequence having at least 80% homology to the amino acid sequence of SEQ ID NO: 1, thus obviating the ground of rejection. Accordingly, the rejection is hereby withdrawn.

Response & Maintained Claim Rejections - 35 USC § 112-Scope of Enablement

Claim 15 and 48-50 stand rejected in modified form under 35 U.S.C. §112, first paragraph, because the specification is not enabling for the full scope of the invention. The rejection set forth on pp. 7-12 of the office action dated December 13, 2007, and pp. 5-7 of the previous office action dated June 11, 2008 is maintained for claim 15 in modified form, for reasons of record.

The specification is considered enabling for a method of screening for a compound or its salt that inhibits the expression of an RNA encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, said method comprising introducing into a nerve cell an antisense molecule or ribozyme to RNA of a gene encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, thereby inhibiting the function of said RNA and inhibiting the neurofibrillary degenerating promoting activity of said protein.

Applicants disagree with the rejection, stating that the Office admits the specification is enabled for a method of screening for a compound or its salt that inhibits the expression of an

RNA encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, said method comprising hybridizing an antisense molecule or ribozyme to RNA of a gene encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, thereby inhibiting the function of said RNA. Applicants additionally state that Applicants' amendment of claim 15 overcomes the rejection. Applicants' arguments have been fully considered, but are not found persuasive.

It is noted that Applicants' amendment of claim 15 fails to limit the claim to the enabled scope previously indicated, or the modified scope presented above. Instant claim 15 encompasses the inhibition of gene expression by any type of drug candidate compound. Further, the method is directed to the culture of any cell type comprising SEQ ID NO: 1, that include non-neuronal cells. Thus, it is not clear how the amendment of the claim has overcome the grounds of the rejection, as the claim clearly encompasses a broader scope than that originally presented, wherein the method was limited to using a polynucleotide. Moreover, it should be noted that the claimed method reads on any cell type, for example a fibroblast comprising the sequence of SEQ ID NO: 1, that would not exhibit any nerve fibers.

As previously noted, the inhibition of gene expression includes inhibition of promoter function either directly, or indirectly by inhibition of transcription factors. The instant specification, while teaching the amino acid of human neuronal cell death inducible putative kinase (NIPK, SEQ ID NO: 1), and the base sequence of DNA encoding the same (SEQ ID NO: 2, p. 69), fails to provide any information regarding the promoter sequences of genomic structure of the human NIPK gene. The specification if further silent on the transcription machinery controlling the expression of human NIPK, and additionally silent on how the transcription of the gene may be inhibited by a candidate compound. Thus, a person of skill in the art would need to engage in further experimentation to discover and characterize the transcription machinery of the human NIPK gene and the sequences controlling promoter activity to design a compound screening method to discover inhibitors of the human NIPK transcription machinery. Such experimentation thus constituting an undue burden on the skilled artisan.

Thus, the previous rejection is maintained for reasons of record and the preceding discussion.

Response & Withdrawn Claim Rejections - 35 USC § 102

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claim 15 and 48-50 were rejected under 35 U.S.C. 102(e) as being anticipated by Meyers et al. (U.S. Patent Application Publication No.: 2002/0034780; filed: Mar. 6, 2001). Applicants' cancellation of claims 48-50 renders their rejection moot. Applicants have amended claim 15 to introduce the step of assaying the degree of changes in nerve fibers, in the claimed method, not expressly taught by Meyers et al. Accordingly, the rejection is hereby withdrawn. Claim 15 is however subject to new rejection over the prior art, as indicated below.

New Claim Rejections - 35 USC § 103

Applicants' claim amendments have necessitated the following new grounds of rejection.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 15 is newly rejected under 35 U.S.C. §103(a) as being unpatentable over Meyers et al. (U.S. Patent Application Publication No.: 2002/0034780; filed: Mar. 6, 2001), in view of Holocomb et al. (Dev. Biol. 172:307-323; 1995).

The rejection has been applied to the extent that the instant claim encompasses an enabled method of screening for a compound or its salt that inhibits the expression of an RNA encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, said method comprising introducing into a nerve cell an antisense molecule or ribozyme to RNA of a gene

encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, thereby inhibiting the function of said RNA and inhibiting the neurofibrillary degenerating promoting activity of said protein.

Meyers et al. describe human kinase nucleic acid sequences and proteins, and methods of using the same (Title and Abstract). Specifically disclosing in Figures 3A and 3B, the amino acid sequences of a human kinase protein (SEQ ID NO: 8), and its corresponding nucleotide sequence (SEQ ID NO: 9), the protein having 100% identity to the instantly claimed SEQ ID NO: 1. The kinase encoded by SEQ ID NO: 8 (also referred to as 13302 protein kinase [¶ 0062]), was found to be similar to rat NIPK neuronal cell-death-inducible putative kinase [¶ 0098]. Meyers et al additionally provide screening methods for identifying a compound that modulates the activity of the kinase protein as well as identifying a compound that modulates the expression of the kinase gene [¶¶ 0022-0024], wherein the compound or agent is a nucleic acid molecule having a nucleotide sequence that is antisense to the coding strand of the kinase mRNA or the kinase gene [¶ 0019]. The antisense nucleic acid molecules, are described as "molecules that are complementary to a sense nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-stranded cDNA molecule, or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire kinase coding strand, or to only a portion thereof, e.g., all or part of the protein coding region (or open reading frame)" [¶ 0180]. Further teaching: "The invention also encompasses ribozymes, which are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Ribozymes (e.g., hammerhead ribozymes (described in Haselhoff and Gerlach (1988) Nature 334:585-591)) can be used to catalytically cleave kinase mRNA transcripts to thereby inhibit translation of kinase mRNA. A ribozyme having specificity for a kinase-encoding nucleic acid can be designed based upon the nucleotide sequence of a kinase cDNA disclosed herein e.g., SEQ ID NOS: 1, 3, 4, 6, 7, 9" [¶ 0185]. Myers et al. additionally describe disorders involving the pancreas as including those of the exocrine pancreas such as diabetes mellitus ¶ [0138], and disorders involving the brain that include, but are not limited to, disorders involving neurons, and disorders involving glia, such as astrocytes, oligodendrocytes, ependymal cells, and microglia ¶ [0122];

While Myers et al. do not describe assaying the degree of neurofibrillary degeneration in their antisense compound screening method, such was known in the prior art.

Holocomb et al. describe the examination of apoptosis in the olfactory epithelium of the mouse and the regulation of neural number (Title and Abstract). Holocomb et al. further describe in vitro culture of neuronal cells and the assessment of their viability using calcein AM staining (as described on p., 32 of the instant specification), and the comparison of neural cell axons in the presence and absence of an apoptotic death inhibitor (Fig. 7, p.317); the axons representing nerve fibers.

The teachings of Meyers et al. and Holcomb et al. all encompass apoptosis inhibitors and their involvement in neurons. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine their respective teachings and to apply the neural apoptosis monitoring and determination method of Holocomb et al., to the compound screening method of Meyers et al., as instantly claimed, with a reasonable expectation of success, at the time of the instant invention. A person of ordinary skill in the art would have been motivated to utilize apoptosis determination method of Holocomb et al. in the method of Meyers et al., because such would allow for the assessment of the effectiveness of the apoptosis inhibitor in neural cell survival.

Applicants should note that the limitation wherein the compound or its salt is a candidate for a prophylactic or therapeutic agent for neurodegenerative disease or diabetes is not afforded patentable weight, because a drug compound may be a candidate for any disease and will remain nothing more than a candidate until proven otherwise. Thus, the limitation of a compound being a candidate for a disease amounts to nothing more than an intended use for the compound. As stated in MPEP 2106, II. Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation. An example of such language includes statements of intended use.

Conclusion

Claim 15 is not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Examiner, Art Unit 1633